Feasibility of using brain attenuation changes on CT to accurately predict time of ischaemic stroke onset

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Feasibility of Using Brain Attenuation Changes on CT to Accurately Predict Time of Ischaemic Stroke Onset

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Background

- Following ischaemic stroke, CT attenuation of affected brain reduces with time
- We piloted whether attenuation of infarct can be used to predict time of stroke onset
- This might enable the safe treatment of ischaemic strokes with intravenous alteplase for patients without a known time of symptom onset

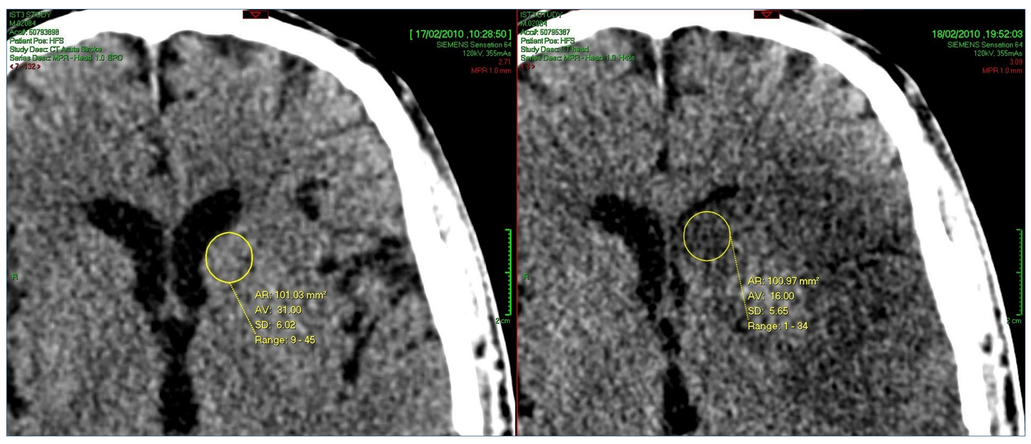

Fig 1. ROI placement within infarct on baseline (left) and follow-up (right) thin-slice CT scans.

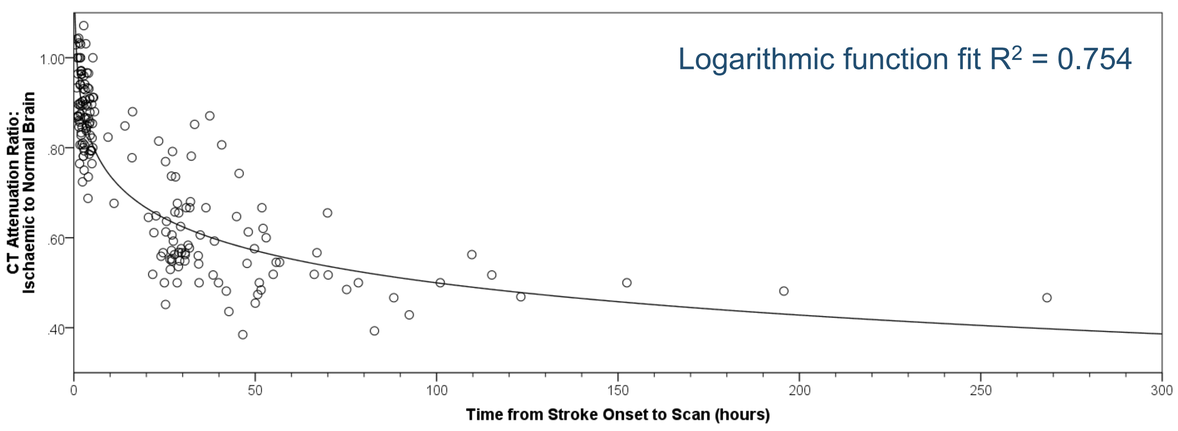

Fig 2. Best-fit logarithmic function for attenuation ratio versus time in the development dataset (n=180).

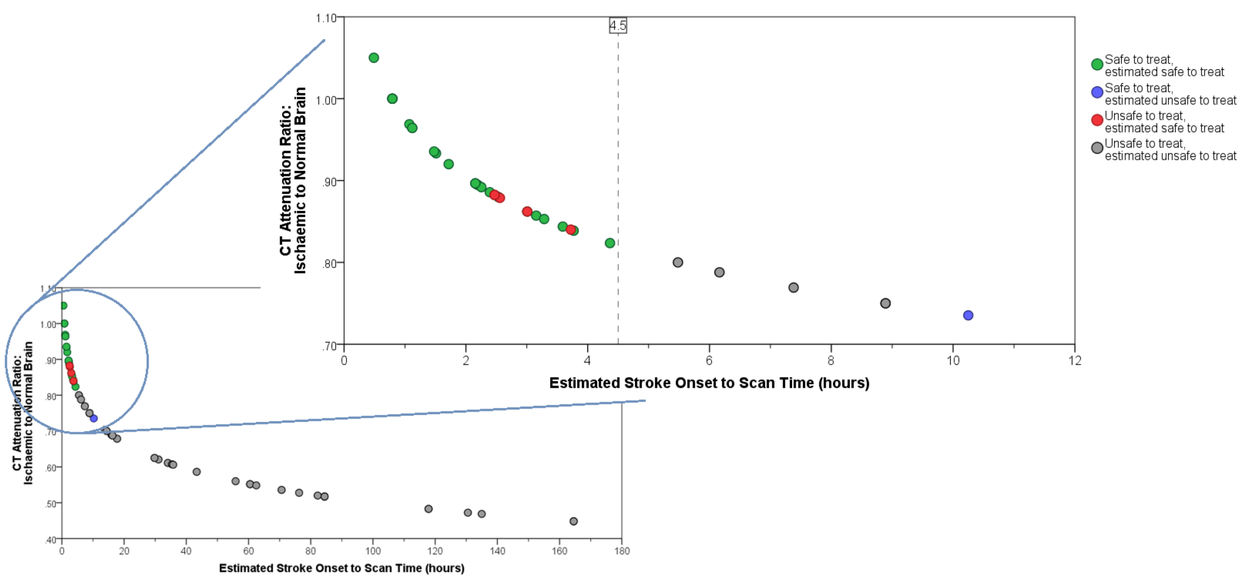

Fig 3. Estimated stroke onset to scan times in the test dataset (n=62), coloured to indicate if suitability for alteplase was correctly estimated. Upper figure highlights time estimates from 0-12 hours (>12 hours, all cases were correctly assessed as unsuitable for alteplase) and indicates 4.5 hour licensing limit for alteplase.

Methods

We selected patients from the Third International Stroke Trial[1] with thin-slice (≤2.5 mm) CT brain imaging available at baseline (<6 hours from stroke onset) and follow-up who had cerebral infarct (but no haemorrhage) visible on their follow-up CT.

A wide range of stroke onset to scan times (time) were selected from among all available baseline and follow-up CT scans.

A neuroradiologist manually applied regions of interest (ROIs) within the infarct and an equivalent contralateral location (normal tissue) at each time point, guided by the infarct location on the follow-up scan (Fig 1).

We derived infarct:normal tissue attenuation ratio .

Cases were assigned to development and testing datasets (75/25%) blind to attenuation ratio.

Attenuation ratio in the development dataset was plotted against time, a best-fit logarithmic function determined (Fig 2) and then used to estimate time in the test dataset.

We assessed accuracy of time estimates and tested the ability of this technique to correctly classify patients as suitable (≤4.5 hours from stroke onset) or unsuitable (>4.5 hours) for intravenous thrombolysis based on current European licensing for alteplase.

Results

- We assessed 242 CT scans from 144 patients
- Among all scans, time ranged from 22 minutes to 268 hours
- There were no significant differences between development and test datasets (Table 1)
- The median percentage error for time estimation in the test dataset was 12.9% (positive value indicates under-estimation)
- Time estimation errors were greatest at extended time periods:
  - 6.8% ≤ 4.5 hours from stroke onset
  - 22.6% > 4.5 hours
- Estimation of patient suitability for treatment with IV alteplase: Sensitivity = 96%, Specificity = 87%, Accuracy = 96% (Fig 3)

Variable	Development Dataset (180)	Test Dataset (62)	P-value for Difference
Age (years)	83 (71-86)	81 (70-85)	0.451
Male Sex	43.7%	40%	0.640
NIHSS	15 (9-20)	15 (10-20)	0.826
Time from stroke onset to scan (hours)	15 (2.7-34.0)	16.7 (2.8-36.8)	0.806
Allocated to alteplase	49.2%	55%	0.463
Attenuation ratio	0.78 (0.56-0.88)	0.75 (0.55-0.88)	0.949

Table 1. Comparison of development and test datasets. Results are median (inter-quartile range) or %.

Conclusions

- These results suggest it might be possible to predict time after stroke onset using only CT brain attenuation
- We have accurately classified patients as suitable or unsuitable for treatment with IV alteplase using this technique
- We plan to validate these findings prospectively in a larger dataset and to test reader reliability

Reference: 1) The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the Third International Stroke Trial [IST-3]): a randomised-controlled trial. The Lancet 2012;379:2352-2363.

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